provided new arguments to the Examiner's rejections based on these claims. Applicant has requested continued examination of the above identified application and requests entry and consideration of this amendment and response. Support for newly added claims can be found on pages 8, 17, 19, and 22 of the specification. Thus, no new matter has been added.

Rejections Withdrawn

The Examiner has withdrawn rejection of claims 1, 3-4 and 6 under 35 U.S.C. 112, second paragraph based on prior amendments in the previously filed response. Although Applicant has cancelled these claims, newly added claims 40-63 reflect the language of claim 1 as previously amended with respect to rejections under 35 U.S.C. 112, second paragraph.

The Examiner has withdrawn rejection of claims 1, 3-4 and 6 under 35 U.S.C. 112, first paragraph based on prior amendments in the previously filed response. Although Applicant has cancelled these claims, newly added claims 40-63 reflect the language of claim 1 as previously amended with respect to rejections under 35 U.S.C. 112, first paragraph.

Objections

Claims 36-38 are objected to for depending from rejected claims. The Examiner suggests that these claims will be allowed if rewritten in independent format. Newly added claims 59-61 correspond to cancelled claims 36-38. Newly added claims 59-61 depend from newly added claim 40.

Rejection of Claims Under 35 U.S.C. § 103(a)

Claims 1, 3-4, 6, 32-35 and 39 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Newman, *et al.* (U.S. Patent No. 5,756,096) in view of Vijh-Warrier, *et al.* (*Molecular Immunology* 32:1081-1092) and Adair, *et al.* (WO 91/09967, published 7/11/91). After consideration of Applicant's argument, the Examiner maintains the

rejection. The Examiner alleges that claims 32-35 and 39 add limitations that would be obvious in view of Adair, *et al.*

In particular, the Examiner alleges that Newman, *et al.* specifically teaches using "chimpanzee constant regions or frameworks." The Examiner goes on to allege that Vijh-Warrier, *et al.* teach using chimpanzee-human chimeric mAbs to reduce immunogenicity. Finally, the Examiner alleges that Adair *et al.* provides motivation to alter framework residues and Newman *et al.*, and Vijh-Warrier, *et al.* provide motivation to use frameworks from Old World Apes.

Applicant has herein cancelled claims 1-39 without prejudice or disclaimer and has added new claims 40-63. Newly added claims are directed to monoclonal antibodies comprising all six CDR regions from a monoclonal antibody produced by a rodent and framework sequences from Old World Ape. Support for antibodies comprising CDRs from rodents and framework residues from Old World Ape can be found in Example 5 (page 17), Example 6 (page 19), and Example 8 (page 22). CDR from both rat and mouse were used to construct chimeric antibodies with Old World Ape frameworks. In addition, support for Old World Ape framework sequences can be found on page 8, lines 18-32 as well as throughout the specification. Applicant respectfully requests consideration of these claims and submits that in submitting these claims Applicant has overcome any rejections of claims 1, 3-4, 6, 32-35 and 39 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Newman, *et al.* (U.S. Patent No. 5,756,096) in view of Vijh-Warrier, *et al.* (*Molecular Immunology* 32:1081-1092) and Adair, *et al.* (WO 91/09967, published 7/11/91).

For a proper obviousness rejection under 35 U.S.C. 103, the Examiner has the burden of establishing *prima facie* with evidence or reasons that, *inter alia*, at the time of the invention, (1) the prior art of record would have suggested or motivated one of ordinary skill in the art to carry out the combination and modification of the prior art as suggested by the

Examiner to arrive at the claimed invention, and (2) "the prior art would also have revealed that in so making or carrying out, those of ordinary skill in the art would have a reasonable expectation of success. Both the suggestion [or motivation] and the reasonable expectation of success must be founded in the prior art, not in the appellants' disclosure." *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991) (citations omitted).

Applicant respectfully submits that Newman, *et al.* is directed to monoclonal antibodies wherein CDRs from Old World Monkeys are combined with a humanized framework. Newman, *et al.* do not teach or suggest the combination of CDRs from rodents with framework from Old World Apes to reduce immunogenicty against a rodent monoclonal antibody. Similarly, Vijh-Warrier, *et al.* is directed to mAbs that are combinations of chimpanzee antibodies with humanized frameworks. The Examiner notes in the Office Action that the findings of Vijh-Warrier, *et al.* suggest, at page 1089, that chimpanzee mAbs are "no more likely to elicit a deleterious anti-immunoglobin response in humans than are human mAbs." However, Vijh-Warrier, *et al.* go on to state that this inference from their findings "emphasizes the potential development of chimpanzee mAbs or chimpanzee-human chimeric mAbs" (page 1089). In other words, both Newman, *et al.* and Vijh-Warrier, *et al.* merely suggest producing mAbs in chimpanzees or Old World Monkeys for reduced immunogenicity and using techniques in the art to humanize these mAbs to reduce immunogencity further. Neither Newman, *et al.* nor Vijh-Warrier, *et al.* suggest developing mAbs in rodents and then altering the framework to resemble that of Old World Ape to reduce immunogencity in humans.

Furthermore, Vijh-Warrier, *et al.* describe infecting chimpanzees with viral and infectious agents to create antibodies for passive immunization of humans (page 1082). Vijh-Warrier, *et al.* direct the skilled artisan to produce antibodies in chimpanzees not in rodents. Newman, *et al.* describe the problem of mouse/human chimeric antibodies generating a

human immunogenic response when used in humans (column 1, lines 44-48). However, Newman, *et al.* do not suggest overcoming this problem by combining rodent CDRs with Old World Ape framework. Instead, Newman, *et al.* suggest combining antigen-binding portions of immunoglobulins from Old World Monkey to human framework. Therefore, neither Newman, *et al.* nor Vijh-Warrier, *et al.* suggest the combination of rodent CDRs with Old World Ape framework, nor do they indicate a reasonable expectation that doing so will successfully produce a rodent antibody with reduced immunogencity in humans.

In addition, Adair, *et al.* is directed to a method of humanizing mAbs from mice to reduce immunogenicity. Adair, *et al.* do not teach or suggest using framework regions or framework substitution corresponding to Old World Ape to reduce immunogenicity to antibodies in humans. Adair, *et al.* merely identify a "hierarchy of positions" within a human framework which are important for obtaining CDR-grafted products with satisfactory binding affinity (page 6). Adair, *et al.* do not teach or suggest that these positions will be similar in Old World Ape, nor do they motivate a skilled artisan to combine CDRs from rodents with framework from Old World Apes with a reasonable expectation of success. For the reasons provided above, Applicant respectfully submits that none of the cited references teach or suggest the instant claimed invention.

Applicant respectfully submits that in view of the forgoing remarks and newly added claims, the Applicant has overcome the Examiner's rejection of claims under 35 U.S.C. §103(a), and that this rejection should be withdrawn.

Applicant reserves the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the claims as originally filed, and any other claims supported by the specification. Applicant thanks the Examiner for the Office Action and believes this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending claims is earnestly solicited.

Attorney Docket: P50770X1C1

If it would expedite the prosecution of this application, the Examiner is invited to confer with the Applicant's undersigned agent.

Respectfully submitted,

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